

REMARKS

1. *Status of claims*

After entry of the above amendment, claims 1-15 and 24-25 are pending, of which claims 5-12 are withdrawn from consideration and claims 24-25 are new. (The office action summary stated claims 5-13 were withdrawn from consideration; Applicants request clarification of the status of claim 13).

2. *Support for amendment*

The above amendment finds support in the specification at p. 21, line 29 to p. 22, line 3, and p. 22, line 30 to p. 23, line 1.

Filed concurrently herewith is a petition under 37 CFR 1.84 to admit color drawings into the application. The replacement Figure 1 attached hereto is an informal copy of the color drawings submitted with the petition.

No new matter has been added by these amendments.

3. *Claim rejections under 35 U.S.C. § 112, first paragraph*

The Examiner rejected claims 1-4 and 13-15 on the ground that the specification, while being enabling for the compound $C_{60}(>C(COOH)_2)_3$, wherein the three $>C(COOH)_2$ moieties are in the C3 conformation (hereinafter, we may refer to this compound as "C3"), does not reasonably provide enablement for all substituted fullerenes listed in groups (i)-(iv) of claim 1. The Examiner also alleged there is insufficient evidence to support claims directed to use of a composition containing C3 to ameliorate a dermatological condition. Applicants traverse this rejection.

The Examiner alleges the treatment and amelioration of dermatological conditions is unpredictable and dependent on many complex chemical and biological factors. However, it is well established in the art that at least some dermatological conditions feature the generation of reactive oxygen species in the skin. For example, Fumelli, *et al.*, *Soc. Invest. Derm.* 115(5):835-841 (2000) ("Fumelli") reports the state of the art regarding sunburn as "[t]he generation of reactive oxygen species and the depletion of cellular antioxidants in the epidermis consequent to [exposure to ultraviolet radiation] has been largely confirmed" and "[t]here is evidence that the formation of sunburn cells is partly mediated by oxygen free-radicals" (p. 835, rt. col., first full paragraph). Also, Fisher, *et al.*, *Arch. Dermatol.* 138:1462-1470 (2002) reports that photoaging by UV irradiation "is initiated by photochemical generation of reactive oxygen species (ROS). Ultraviolet-induced ROS also cause direct deleterious chemical modifications to cellular components" (Abstract, p. 1462).

The present specification and figures, including Example 1 and the replacement sheets of Figure 1 attached hereto, indicate that a substituted fullerene ameliorated sunburn in a test subject (inventor Wilson). Given that substituted fullerenes have antioxidant activity, as discussed in Example 2, the skilled artisan would conclude that the antioxidant activity of the substituted fullerene of Example 1 led to the amelioration of the sunburn in the test subject.

Because the various substituted fullerenes discussed in Example 2 have antioxidant activities from about 2-fold greater to about 70-fold less than that of Trolox, a known comparative antioxidant (as indicated by their IC₅₀ values in the xanthine/xanthine oxidase/cytochrome c system discussed in Example 2), the skilled artisan would further conclude that the any of the substituted fullerenes discussed in Example 2 would have ameliorated the sunburn in the test subject and, further, that any of the substituted fullerenes recited by claim 1

and having substituent structural features in common with a substituted fullerene discussed in Example 2 would have similar antioxidant activities with a substituted fullerene discussed in Example 2 and therefore would also have ameliorated the sunburn in the test subject.

Although sunburn is only one dermatological condition, the generation of reactive oxygen species occurs in the course of at least one other dermatological condition, photoaging (Fisher, *supra*). In addition, the skilled artisan would find it a routine matter to determine whether reactive oxygen species are generated or cellular antioxidants are depleted in the course of another dermatological condition. If they are, then the skilled artisan would find it a routine matter to determine whether quenching of reactive oxygen species by addition of a substituted fullerene would ameliorate the dermatological condition.

Therefore, Applicants submit the specification is enabling for the use of a substituted fullerene listed in groups (i)-(iv) of claim 1, such as C3, to ameliorate a dermatological condition. Applicants request this rejection of claims 1-4 and 13-15 be withdrawn.

4. *Claim rejections under 35 U.S.C. § 102(b)*

The Examiner rejected claims 1-4 and 15 as being anticipated by Fumelli. Applicants traverse this rejection.

Fumelli teaches the administration of carboxyfullerenes, such as C3, to cultured keratinocytes *in vitro*, as preventing UVB-induced inhibition of keratinocyte proliferation and UVB-induced keratinocyte apoptosis (Materials and Methods, pp. 835-836, and Results, pp. 838-839 and Figs.2-5). Fumelli is silent regarding whether carboxyfullerenes would be effective *in vivo* in ameliorating dermatological conditions. Fumelli is silent regarding whether carboxyfullerenes would be effective in entering the skin of a living subject. In contrast, the

present claims recite methods of ameliorating dermatological conditions which involve administering a substituted fullerene to the skin of a subject, with entry of the substituted fullerene into the skin being demonstrated by Example 1 and Fig. 1. Therefore, Fumelli does not teach every element of the present claims and thus cannot anticipate them. Applicants therefore request this rejection of claims 1-4 and 15 be withdrawn.

5. *Conclusion*

Applicants submit all pending claims are in condition for allowance. The Examiner is invited to contact the undersigned patent agent at (713) 934-4065 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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